REMARKS

Preliminary Remarks

Claims 89, 102-111, and 117-121 are currently pending and are under the examination. Claims 1-88 are canceled. Claims 89, 102, and 107 are amended with this response. Claims 117-121 are newly presented. Support may be found for examples on page 4 and 5 of the specification.

Patentability Arguments

A. The Rejections of Claims 89, 102-103, 105-108 and 110 Under 35 U.S.C. § 102(a) as Being Inherently Anticipated by WO 98/39361

At page 2 of the Office action, the Examiner rejected claims 89, 102-103, 105-108 and 110 allegedly because the claims are inherently anticipated by Bram PCT WO98/39361 ("Bram PCT"). The claims are amended with this response. Claim 89 is amended by inserting a clarifying term "a ligand binding fragment of a soluble form of a ztnF4 receptor.

In rejecting the claims, the Examiner quotes *In re Best,* which held that "it is elementary that the mere recitation of a newly discovered function or property, inherently possessed by things in the prior art, does not cause a claim drawn to those things to distinguish over the prior art." *In re Best*, 562 F.2d 1252, 1254 (C.C.P.A. 1977) (Emphasis added).

In response, the Applicants reiterate and incorporate by reference all of the arguments made in response to this rejection made earlier during prosecution of this application.

Briefly, Bram PCT does not teach a method of inhibiting B cell proliferation by using a ligand binding fragment of a ztnF4 receptor that binds ztnF4 and further does not describe the specific fragments presently claimed. In fact, in line 19 of page 52 of the specification, Bram PCT specifically states that "the identity of the endogenous ligand of the TACI protein (a ztnF4 receptor) is unknown." Bram then teaches how the TACI protein can be used in different assays to identify ligands for this receptor.

At pages 4-5 of the office action, the Examiner alleges that "since the fusion proteins disclosed by Bram PCT are identical to those of the instant invention, said fusion proteins would possess all of the same properties as those of the instant invention (including the ability to bind the ztnF4 ligand)." Applicants bring to the Examiner's attention that the fusion proteins disclosed by Bram PCT are not identical to those claimed in the presently amended claims. The

instant claims now recite "a ligand binding fragment soluble term of a ztnF4 receptor and after claim recites specification fragments of the receptor." Bram PCT teaches an extracellular domain of TACI, but it does not and cannot identify more specifically which portion of the extracellular domain of a TACI is required for the interaction with ztnF4 because TACI ligands were not known at the time of Bram PCT disclosure.

At page 4 of the Office action, the Examiner also alleges that Bram PCT teaches in lines 1-6 of page 8 that fusion proteins intercept the normal endogenous ligands (*i.e.*, ztnF4) that serve to cross-link and activate the TACI proteins on the surface of cells thus inhibiting the ligand's activity. Bram PCT in pertinent part reads as follows:

> "The present invention also includes the preparation of a recombinant form of the extracellular portion of a TACI protein. . . This component intercepts the normal endogenous ligands which serve to crosslink and activate the TACI protein. . . Such administration is useful in the treatment or prevention of autoimmune disease or graft-rejection or graft-vs-host disease following transplantation."

The quote does not disclose fusion proteins. The quote does not disclose ztnF4, fusion proteins that intercept ztnF4 or ligand binding fragment of a soluble ztnF4 receptor that bind to ztnF4. Instead, it states a general scientific hypothesis that the extracellular domain of a TACI may intercept the endogenous ligands of the TACI which Bram PCT admits were not known at the time of its disclosure.

For the reasons stated above, applicants submit that Bram PCT does not satisfy the standard for an inherent disclosure and therefore, the Examiner may properly withdraw the rejection of instant claims over Bram PCT under 35 U.S.C. §102 (a) and such withdrawal is requested.

- **The Rejections Under 35 U.S.C. § 102(e) as Being Inherently Anticipated by U.S. Patent No. 5,969,102 Should Be Withdrawn**

At page 5 of the Office action, the Examiner rejected claims 89, 102-103, 105-108, and 110-111 allegedly as being inherently anticipated by U.S. Patent No. 5,969,102 ("Bram US"). In response, the Applicants reiterate and incorporate by reference all arguments made during the prosecution of this application.

Applicants further note that on page 7 of the office action, the Examiner asserts that in line 64 at column 13, Bram US discloses that the "subunits" of TACI and the Fc domain can be linked by peptide bonds. Bram US in pertinent part states as follows:

> The term "polypeptide" is used in its broadest sense to refer to **a compound of two or more subunit amino acids**, amino acid analogs, or peptidomimetics.
>
> The subunits may be linked by peptide bonds. In another embodiment, the subunit may be linked by other bonds, e.g., ester, ether, etc. As used herein the term "amino acid" refers to either natural and/or unnatural or synthetic amino acids, including glycine and both the D or L optical isomers, and amino acid analogs and peptidomimetics. A peptide of three or more amino acids is commonly called an oligopeptide if the peptide chain is short. If the peptide chain is long, the peptide is commonly called a polypeptide or a protein.

The quote simply does not disclose a fusion of a ztnF4 receptor and Fc let alone a fusion of a ligand binding fragment of a soluble ztnF4 receptor or the particular fragment presently claimed.

The Examiner also alleges that Bram US in column 5, lines 45-53, discloses fusion proteins that intercept the normal endogenous ligands that serve to cross-link and activate TACI protein and therefore inhibiting the ligands activity. Bram US in a pertinent part provides as follows:

> The present invention also includes the preparation of a recombinant form of the extracellular portion of a TACI protein, thereby creating a dominant-negative or blocking reagent. This component intercepts the normal endogenous ligands which serve to crosslink and activate the TACI protein. Administration of such a polypeptide acts to suppress the immune system. Such administration is useful in the treatment or prevention of autoimmune disease or graft-rejection or graft-vs-host disease following transplantation.

As discussed above, the quote again does not disclose fusion proteins let alone a ligand binding fragment a soluble ztnF4 receptor fused to an Fc. Further, the quote does not disclose the ligand ztnF4. The quote does not disclose methods of inhibiting B cell proliferates using molecules as presently claimed.

On page 8 of the office action, the Examiner alleges that fusion proteins disclosed in the quoted passage are identical to those of the instant claims and would possess the same properties of the instant invention. Applicants submit that there are no fusion proteins disclosed in the passage but only that a recombinant form of the extracellular portion of a TACI is disclosed. The instant claims, as amended, are directed to methods of inhibiting B cell proliferation with

fusion proteins comprising a ligand-binding fragment of a soluble ztnF4 receptor not taught by Bram US. The applicants submit that as a matter of law, Bram US cannot properly anticipate the present invention.

B. <u>The Rejections of Claims 89 and 102-111 Under 35 U.S.C. § 103 Should be Withdrawn Over Bram (PCT) in View of Presta, Should be Withdrawn</u>

At page 9 of the Office action, the Examiner rejected applicants' claims as being obvious over Bram PCT in view of U.S. Patent No. 5,739,277 (Presta).

The Examiner reiterates the argument set forth in rejection of the claim under 102(a) and (e) in view of Bram PCT and U.S. Patent No. 5,969,102 and combines it with Presta to provide disclosure of fusion proteins which comprise Fc fragments.

For the reasons stated above (section A, above), applicants submit that fusion proteins of the instant claims are not identical to those of Bram PCT. Bram PCT did not and could not teach fusion proteins comprising a ligand-binding fragment of a ztnF4 receptor as presently claimed and further could not have identified such a fragment because the ligand ztnF4 was not known.

Further, Presta does nothing to render the failure of Bram. Presta deals with methods of improving recombinant protein stability by, for example, fusing the protein to an Fc fragment of an antibody.

In summary, because Bram PCT fails to teach or suggest limitations of the instant claims and because Presta fails to overcome that failure, therefore, the combination cannot as a matter of law render the instant claims obvious and the rejection over Bram PCT in view Presta under 35 U.S.C. § 103(a) should be withdrawn, and the withdrawal is respectfully requested.

- **The Rejection over Bram US in view US patent 5,739,277 (Bram US) to Presta et al. (Presta) Should Be Withdrawn**

The Examiner has also maintained the rejection of claims 89 and 102-111 rejection under 35 U.S.C. 103(a) as being unpatentable over Bram US in view of Presta.

In advancing his rejection, the Examiner argues that Bram US/Presta combination makes the instant claims obvious because Bram US teaches fusion proteins identical to those of the

instant invention and Presta discloses the Fc portions of the various immunoglobulins with increased half-life.

As discussed in more detailed above, Bram US does not disclose a ligand binding fragment of a soluble ztnF4 receptor fused to an Fc as is called for by the present claims. Further, while Presta does teach the use of Fc fragments of antibodies to increase the stability of protein, it does not remedy the failure of Bram to teach or suggest the molecules recited in the present claims.

In summary, because Bram PCT fails to teach or suggest the present invention and because Presta fails to overcome that failure, therefore, the combination cannot as a matter of law render the instant claims obvious and the rejection over Bram PCT in view Presta under 35 U.S.C. § 103(a) should be withdrawn, and the withdrawal is respectfully requested.

C. The rejection of claim 89 and 102-111 under 35 U.S.C. § 112, first paragraph should be withdrawn.

The Examiner has maintained the rejection of the claims under 35 U.S.C. § 112, first paragraph, for allegedly failing to describe at least substantial numbers of what the Examiner characterizes as a "vast genus of soluble forms of ztnF4 receptors" and alleges that the specification does not disclose distinguishing and identifying features of a representative number of members of at least a substantial number of the members of the claimed genus.

The Applicant respectfully traverses the rejection and requests reconsideration in view of the following. The specification recites detailed structural features (by way of sequence), identifies the soluble form of at least three ztnF4 receptors including BR43x2, TACI and BCMA and has provided the explicit definition of the particular fragments of those soluble forms as set out in the present claims and described in the specification. The applicants submit that the genus of such soluble domains of a ztnF4 receptor is not in fact vast and is fully supported by the description set out in the specification.

In view of the foregoing, the Applicant submits that the claims fully comply with the written description requirement of 35 U.S.C. § 112, first paragraph and thus this rejection should be withdrawn.

Conclusion

In view of the above amendments and remarks, applicants respectfully submit that the instant application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is encouraged to call the undersigned at the (312) 595-1408. Should any additional fees be deemed necessary in connection with the filing of this document, the Commissioner is hereby authorized to deduct any such fees from Deposit Account No. 08-3038 referencing the above attorney docket number.

Respectfully submitted,

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